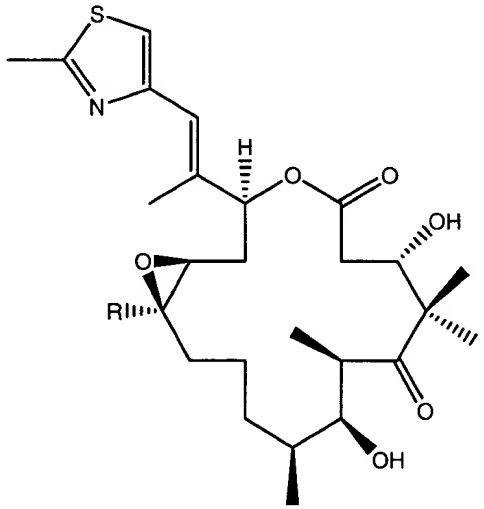
Please cancel claims 30 and 59-143, without prejudice. For the convenience of the Examiner, a copy of the complete set of pending claims, in the form that they will take after entrance of the present Amendment, is included herewith at the end of the Response.

II. Addition of Claims:

Please add the following new claims 144-160:

--144. (New) A pharmaceutical composition for delivering a therapeutically effective amount of a compound to a mammal, the pharmaceutical composition comprising: an amount of a compound and a therapeutically acceptable carrier, wherein the compound has the structure:



wherein R is hydrogen or methyl; and

wherein the amount of the compound in carrier is sufficient for the composition to deliver to the mammal between about 0.001 mg to about 40 mg compound pre kg body weight.

145. (New) The pharmaceutical composition of claim 144, wherein R is hydrogen.

146. (New) The pharmaceutical composition of claim 144, wherein R is methyl.

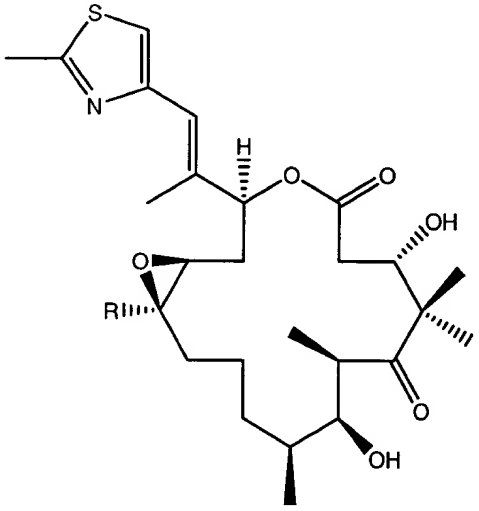
147. (New) The pharmaceutical composition of any one of claims 144-146, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.01 mg to about 40 mg compound per kg body weight.

148. (New) The pharmaceutical composition of any one of claims 144-146, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.001 mg to about 25 mg compound per kg body weight.

149. (New) The pharmaceutical composition of any one of claims 144-146, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.01 mg to about 25 mg compound per kg body weight.

150. (New) A method of treating cancer in a subject comprising:

administering to the subject in need thereof a therapeutically effective amount of a compound having the structure:



wherein R is hydrogen or methyl; and

wherein the therapeutically effective amount of the compound is an amount between about 0.001 mg to about 40 mg compound per kilogram of the subject's body weight.

151. (New) The method of claim 150, wherein R is hydrogen.

152. (New) The method of claim 150, wherein R is methyl.

153. (New) The method of any one of claims 150-152, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.01 mg to about 40 mg compound per kg body weight.

154. (New) The method of any one of claims 150-152, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.001 mg to about 25 mg compound per kg body weight.

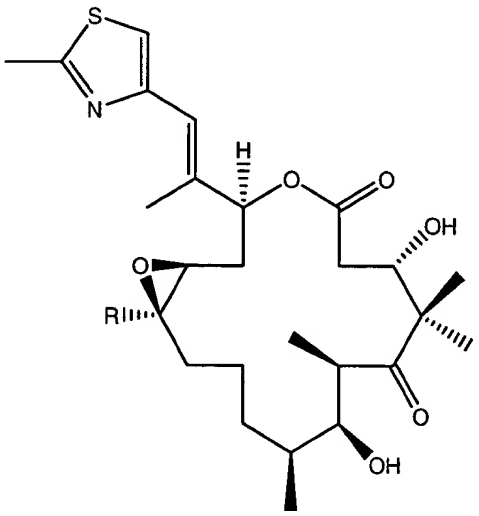
155. (New) The method of any one of claims 150-152, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.01 mg to about 25 mg compound per kg body weight.

156. (New) The method of any one of claims 150-152, wherein the composition is administered to the subject at least twice in a seven-day period.

157. (New) The method of any one of claims 150-152, wherein the step of administering comprises:

administering in at least two does a therapeuticall effective amount of the compound to a subject in need thereof, wherein the therapeutically effective amount of the epothilone is an amount sufficient to deliver about 0.001 mg to about 40 mg epothilone per kilogram body weight.

158. (New) A method of inhibiting growth of a tumor in an animal comprising: administering to an animal that has a tumor an amount of a composition comprising a compound having the structure:



wherein R is hydrogen or methyl;

wherein the amount being effective to inhibit growth of the tumor without administration of the composition killing the animal; and

wherein the amount of the composition is an amount sufficient to deliver about 0.001 mg to about 40 mg epothilone per kilogram body weight.

159. (New) The method of claim 158, wherein R is hydrogen.

160. (New) The method of claim 158, wherein R is methyl.--

III. Rejection of claims 30 and 59-94 under 35 U.S.C. § 103(a):

The Examiner has rejected claims 30, 59-64, 69, 71-77, 82-101, 106, 108-119, and 124-143 under 35 U.S.C. § 103(a) as being unpatentable over the Bollag *et al.* reference (*Cancer Res.*, Vol. 55 (1995), pages 2325-2333). The Examiner asserts that the Bollag *et al.* reference teaches "epothilones A (wherein R is H) and B (R is methyl), their compositions as an oily residue (column 2, page 2326) and methods of use for treating cancer or tumor cells and particularly multiple drug-resistant cells. (See column 2, page 2331)." The Examiner further asserts that the Bollag *et al.* reference teaches "the method of use of epothilones in combination with taxol (a cytotoxic agent). See column 2, page 2328 to column 1, page 2330." In the section entitled "Ascertainment of the difference between the prior art and the claims" the Examiner

states that "the difference between the instant invention and the disclosure of Bollag *et al.*, is that applicants substitute methyl, ethyl, or propyl for H at position R." Examiner continues that "applicants are also claiming effective amounts of epothilones from about 0.001 to about 1 mg/kg of body weight, and administration of the effective dose to a subject multiple times." In the section labeled "Finding of *prima facie* obviousness—rational and motivation" the Examiner then asserts that "for the Bollag *et al.,* to use epothilones for the treatment of cancer or tumors, effective amount must necessarily be used," and states that Applicant's "claiming variable effective amounts of epothilones, and administration of the effective dose to a subject multiple times, is not in and of itself patentable over the prior art of Bollag *et al.*" The Examiner further states that "the motivation is in the expectation that the epothilone compositions would be effective for the treatment of cancer given the experimentation performed by Bollag *et al.*, and the results."

Applicant respectfully traverses this rejection. Bollag *et al.* demonstrates that Epo A and Epo B are cytotoxic to certain cultured cell lines including HeLa cells, Hs578T cells, and multiple-drug resistant cells. Many compounds are cytotoxic in such *in vitro* studies. Precious few prove to be useful as therapeutics. Most typically, the difficulty with cytotoxic compounds is that it is not possible to administer them in an amount that will kill tumor cells without also killing the host organism. Thus, the teachings of Bollag *et al.* provide, *at most* a suggestion that it might be desirable to *try* to find an amount of an epothilone that could be therapeutically effective. There is no reasonable expectation that such an amount exists and can be found. As discussed in the prior Response of July 16, 2002, the Bollag *et al.* reference itself viewed their own results as an invitation to experiment and not a demonstration of a pharmaceutically useful or effective composition.

Furthermore, as discussed in the in-person interview on November 19, 2002, the present inventors, who are of at least of ordinary skill in the art, could not readily identify a therapeutically effective range of Epo A or Epo B based on Bollag *et al*'s description, which does not even suggest a therapeutically effective concentration of epothilone necessary to treat cancer in a subject. Using *in vivo* studies in mice, Applicant did discover a therapeutically effective range from about 0.001 mg to about 40 mg epothilone per kg body weight. Initial studies of administering epothilone compounds to mice led unexpectedly to all the mice being